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Quantum biology

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Recent evidence suggests that a variety of organisms may harness some of the unique features of quantum mechanics to gain a biological advantage. These features go beyond trivial quantum effects and may include harnessing quantum coherence on physiologically important timescales. In this brief review we summarize the latest results for non-trivial quantum effects in photosynthetic light harvesting, avian magnetoreception and several other candidates for functional quantum biology. We present both the evidence for and arguments against there being a functional role for quantum coherence in these systems.

Before the twentieth century, biology and physics rarely crossed paths. Biological systems were often seen as too complex to be penetrable with mathematical methods. After all, how could a set of differential equations or physical principles shed light on something as complex as a living being? In the early twentieth century, with the advent of more powerful microscopes and techniques, researchers began to delve more deeply into possible physical and mathematical descriptions of microscopic biological systems[1]. Some famous examples[1–3] (among many) include Turing patterns and morphogenesis, and Schrödinger's lecture series and book 'What is Life?', in which he predicted several of the functional features of DNA. The pace of progress in this field is now rapid, and many branches of physics and mathematics have found applications in biology; from the statistical methods used in bioinformatics, to the mechanical and factory-like properties observed at the microscale within cells.

This progress leads naturally to the question: can quantum mechanics play a role in biology? In many ways it is clear that it already does. Every chemical process relies on quantum mechanics[3]. However, in many ways quantum mechanics is still a concept alien to biology, especially on a scale that can have a physiological impact[4]. Recent technological progress in physics in harnessing quantum mechanics for information processing and encryption puts the question in a different light: are there any biological systems that use quantum mechanics to perform a task that either cannot be done classically, or can do that task more efficiently than even the best classical equivalent? In other words, do some organisms take advantage of quantum mechanics to gain an advantage over their competitors? Many attempts to find examples of such phenomenon have been met with fierce criticism by both physicists and biologists (see, for example, refs 5,6). However, over the past decade a range of experiments have suggested that there may be some cases in which quantum mechanics is harnessed for a biological advantage. In what form do these quantum effects usually appear? In quantum information, arguably the most important quantum effect is that quantum bits can exist in superpositions whereas classical bits cannot. In quantum biology, the role of quantum effects can be subtle and will be described for each system we discuss in this review. However, we may consider a biological system that exploits coherent superpositions of states for some practical purpose to be the clearest example of functional quantum biology. Some of the systems we discuss are thought to fit into this category, but not all.

Here we present a very brief overview of some of these cases in which quantum effects may assist or enhance a biological function. Our goal is to give a clear basic introduction to each system and to outline in what way quantum coherence or other quantum effects might be harnessed by this system. We also attempt to present the latest evidence both for and against these quantum effects actually being functional. We begin by discussing the observation of quantum coherence (superpositions) at room temperature in the transport of excitation energy through photosynthetic systems. We briefly summarize the latest research about the role this coherence might play in the efficiency of photosynthesis in bacteria and plants. We then move onto an entirely different system: the radical-pair model used to describe the magnetic sense of some avian species. The evidence supporting the radical-pair model is primarily based on behavioural experiments, although very recent *in vitro* experiments[7] on candidate radical pairs are in its favour. The possibility that a macroscopic cognitive species could respond to fundamentally quantum effects is fascinating, but a cautious approach of course needs to be taken to fully verify and understand this phenomenon. Finally, we will briefly discuss several other biological functions in which quantum mechanics may play a vital but less direct role, including long-range tunnelling of electrons through proteins and the rapid photoisomerization in photoreceptors. Some of these last examples could be considered as a class of quantum phenomena in biological systems that depends only on trivial quantization and discrete energy levels, not on quantum coherence. A brief list of selected works that demonstrate quantum effects in the examples we discuss here is shown in Table 1.

Quantum coherent energy transport in photosynthesis

Photosynthesis provides energy for almost all life on Earth. This energy, in the form of photons, is absorbed by light-harvesting antennas as an electronic excitation[8,9]. This excitation is then transported from each antenna to a reaction centre where charge separation creates more stable forms of chemical energy. The precise biological structures and pigment constituents used, from the antenna to the reaction centre and onwards, vary between organisms[9,10]. For example, purple bacteria use highly symmetric

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Table 1 | Summary of a selection of the main experimental and theoretical works on functional quantum biology.

Biological system		Reference
Photosynthesis	Cryogenic-temperature quantum coherence	12,14
	Ambient/room-temperature quantum coherence (FMO)	16
	Ambient/room-temperature quantum coherence (algae)	15
	Environment-assisted transport	19,26,27,29
	Entanglement, tests of quantumness	48,49,103
	Alternative views	46,47,51
Radical-pair magnetoreception	Early proposals and evidence	60,66
	Mathematical models	66,67
	Indirect evidence (light dependence, magnetic field)	58,61,64,65,78,104
	Experiments on radical pairs	7,71–73,105
Other examples	Olfaction	92,93
	Vision	97,99
	Long-range electron transfer	81,82
	Enzyme catalysis	84,85

ring-like structures for light harvesting[11], whereas green plants and cyanobacteria have photosystems with chlorophylls (light-absorbing pigment molecules) that seem to be randomly arranged. Moreover, most photosynthetic organisms use arrangements of such chlorophyll molecules complexed with proteins, but cyanobacteria and red algae use a unique chromophore called a phycobillin. This diversity in light-harvesting apparatus reflects the necessity for photosynthetic organisms to adapt in response to different physiological conditions and natural habitats[10]. One of the simplest and most well-studied examples is the light-harvesting apparatus of green-sulphur bacteria (Fig. 1). These have a very large chlorosome antenna that allows them to thrive in low-light conditions. The energy collected by these chlorosomes is transferred to the reaction centre through a specialized structure called the Fenna–Matthews–Olson (FMO) complex. Owing to its relatively small size and solubility in water, the FMO complex has attracted much research attention and as a result has been well characterized. What is remarkable is the observed efficiency of this and other photosynthetic units. Almost every photon (nearly 100%) that is absorbed is successfully transferred to the reaction centre, even though the intermediate electronic excitations are very short-lived (~1 ns). In 2007, Fleming and co-workers demonstrated evidence for quantum coherent energy transfer in the FMO complex[12], and since then the FMO protein has been one of the main subjects of research in quantum biology.

The FMO complex itself normally exists in a trimer of three complexes, of which each complex consists of eight bacteriochlorophyll *a* (BChl-*a*) molecules. These molecules are bound to a protein scaffold, which is the primary source of decoherence and noise, but which also may assist in protecting the coherent excitations in the complex and play a role in promoting high transport efficiency[13]. The complex is connected to the chlorosome antenna through what is called a baseplate. Excitations enter the complex from this baseplate, exciting one of the BChl molecules into its first singlet excited state. The molecules are in close proximity to one another (roughly 1.5 nm), enabling the excitation energy to transfer from one BChl molecule to another, until it reaches the reaction centre.

Quantum properties. As mentioned, direct evidence for the presence of quantum coherence over appreciable length scales and timescales in the FMO complex was observed by Engel *et al.*[12] in 2007. They presented the spectroscopic observation, at low temperature (77 K), of quantum coherent dynamics (that is, coherent superpositions evolving in time) of an electronic excitation across multiple pigments within the FMO complex. Since that time a huge body of literature has arisen, and further experiments[14–17] suggest that the coherence is non-negligible even at room temperature, for up to 300 fs. If quantum coherent dynamics are present at room temperature in the FMO complex (and other parts of a light-harvesting apparatus), what purpose does it serve? As we will discuss in the next section, a higher transport efficiency[18] is the typical answer, and a large variety of theoretical models have been employed to explain if, how and why nature uses quantum coherence to move this electronic excitation through the FMO complex[19] more efficiently than classically possible. The closest equivalent classical model against which one can compare such quantum effects is the Förster model that treats the transfer of the excitation between sites as an incoherent rate, and neglects all coherences or superpositions between sites. One should also note that the excitonic nature of the system, manifested in the coherent delocalization of photoexcitation among several molecular sites, is also important and strongly influences the spectroscopic properties and energy relaxation of the complex, which should be discussed independently[20–22].

At first the notion of observing quantum coherence at room temperature in a biological system may be quite surprising. However, even a naive comparison[23,24] of the relevant energy scales suggests that in fact quantum effects could be important in this case. These energy scales are the environment's temperature (~300 K), the coupling strength between the excitation in the FMO complex and the protein environment (~100 cm^{-1}) and the electronic coupling strength that transfers the excitation between BChl molecules (~100 cm^{-1}). Precisely calculating or measuring the energies and coupling strengths in a photosynthetic complex such as FMO requires a combination of spectroscopy and *ab initio* quantum chemistry methods based on atomistic models[23,24]. Fortunately FMO is one of the most well-studied models, and generally speaking both measurements and calculations of the coupling strengths and energies agree quantitatively[25].

Environment-assisted transport. One can argue that the goal of the FMO complex is to maximize the efficiency of transporting a single excitation from the BChl-*a* molecule nearest the antenna to the BChl-*a* nearest the reaction centre (see Fig. 1). To this end, apart from the energy and couplings mentioned earlier, there are two other important timescales to be considered. One is the rate at which the excitation leaves the target molecule and enters the reaction centre (~1 ps). The other is the rate at which the excitation in any of the BChl is lost owing to fluorescence relaxation (~1 ns). It is this latter rate that the excitation must beat, in its race to reach the reaction centre. Remarkably, the excitation is almost

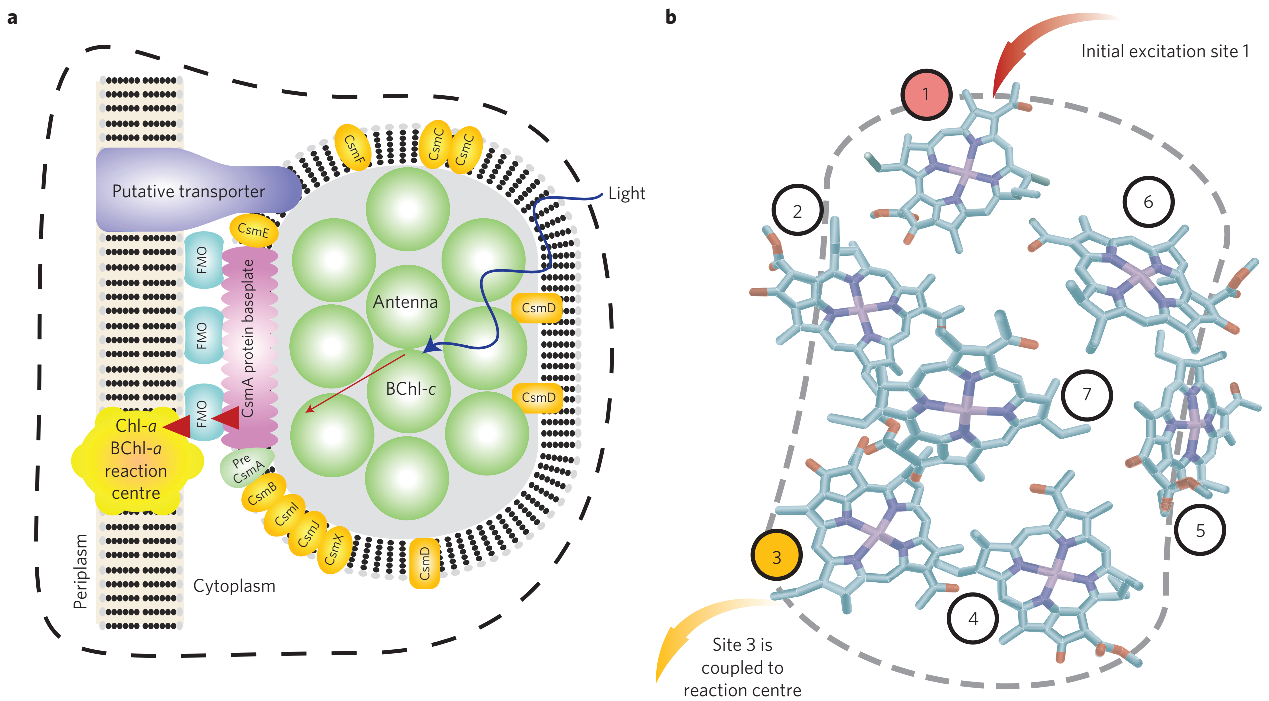


Figure 1 | A quantum machine for efficient light-energy harvesting. The well-studied FMO complex in the light-harvesting apparatus of green-sulphur bacteria exhibits some signatures of quantum coherent energy transfer. Experimental and theoretical works have scrutinized the precise mechanisms and quantumness of the energy transduction through this protein. Research in this field might reveal new quantum mechanical principles for improving the efficiency of energy harvesting in biology. **a**, Diagram of the photosynthetic apparatus of green sulphur bacteria, including its antenna, energy-conducting baseplate and FMO complexes, and reaction centre. The chlorosome antenna (green discs) is composed of roughly 200,000 BChl-*c* molecules, and is an exceptionally large structure that is designed to capture as many photons as possible in the low-light conditions the bacteria thrive in. Sunlight creates an excitation in this antenna that is transferred (red arrows) to the reaction centre through one of several FMO complexes. **b**, The BChl-*a* arrangements of one of the FMO pigment-protein complexes through X-ray diffraction. The FMO complex comprises eight (although only seven are shown here) bacteriochlorophyll-*a* (BChl-*a*) molecules that are encased in a protein scaffolding (not shown). The excitation arrives from the chlorosome at one of the sites, typically thought to be the site denoted as 1. This excitation is then transported from one BChl molecule to the next. Once it arrives at site 3 it can irreversibly enter the reaction centre and start a charge-separation process.

always transferred to the reaction centre faster than it can be lost to fluorescence relaxation.

How then might quantum coherence in the transport process help the excitation get to where it needs to go? Several physically plausible explanations have been proposed. Some theoretical approaches focused on treating the protein environment as a Markovian and uncorrelated thermal bath. This meant that each site in the FMO complex feels its own individual random environmental noise. Such treatments[26,27] suggest that the combination of the coherence of the excitation transport and the thermal environment creates a level-broadening effect. Simple models[19,26–28] predict that this allows the excitation to easily escape any local minima in the uneven excitation energy landscape of the FMO complex. Other authors[29] have demonstrated that the coherent dynamics of the excitation can also conspire with the rapid (incoherent) rate of transfer from the site closest to the reaction centre to the reaction centre itself. They showed that this collaboration between quantum coherent evolution and incoherent tunnelling creates a high-efficiency energy trap, drawing the excitation into the reaction centre.

Recent progress. Much of the latest theoretical work on the FMO complex has been on the nature of the protein environment. As mentioned earlier, the simplest treatment is to consider each molecule to be in contact with an uncorrelated Markovian thermal bath. However, because of the strong coupling (100 cm^{-1}) between the electronic excitations and nuclear motion in the protein environments around the FMO (refs 30,31) complex, the consensus is that this treatment is insufficient. There are three approximations that may break down in this limit: the perturbative-coupling approximation (sometimes termed the Born approximation in system–bath models), the memory-less (or Markovian) approximation and the independent-bath approximation. A great deal of work has been done on understanding what happens when these three approximations are relaxed[13,19,31–38].

Evidence, both theoretical and experimental, does hint that the non-perturbative and non-Markovian environment can enhance both the coherence time[19] and the efficiency of the excitation transport[39]. Similarly, a recent analysis argued that coherent vibronic excitations may play an important role in the coherent oscillations seen in experiments[40–42]. However, the role of correlations between the baths of different BChl molecules is still not fully understood. Recent work[39] showed that the correlations can in principle improve the efficiency in some cases, but can also decrease it, and that there is an optimal overall noise level. In comparison, molecular dynamics simulations[43,44] indicated that the uncorrelated-bath approximations may hold, and thus independent-bath models may be sufficient to explain any enhancement in efficiency. Ultimately, the real role of correlated-bath effects and vibronic excitations in photosynthetic units, FMO and otherwise, is still not clear, and requires further experimental studies.

Despite the positive results and predictions we discussed in the last section, recent analysis has shown that the efficiency benefits provided by quantum models in comparison to the classical Förster model (which can be seen as a perturbative expansion of the quantum one, with no quantum coherence) may be only a few

per cent[45]. However, even a few per cent improvement in efficiency may be vital for a plant or bacteria attempting to survive in low-light conditions. Is the Förster model the only classical model against which we should compare efficiencies? For example, recent work[46,47] proposed an alternative model of the type of transport that occurs in the FMO complex that predicts oscillations and quantum-like behaviour, but is entirely classical. Several studies[48,49] have proposed ways to unambiguously verify that quantum effects are the correct way to describe the observed experiments, although they are as yet beyond experimental implementation.

One should also note that most of these results omit the recently discovered eighth BChl-*a* molecule[50]. Ritschel *et al.*[36] recently studied the full FMO trimer, including the eighth BChl molecule in each complex in the trimer. They found that if one considers this new molecule as the site that accepts the excitation from the antenna (which may be the case because it is located close to the baseplate) almost no coherent exciton dynamics occur because of its weak coupling and large energy detuning to the other sites. In this case they observed only exponential decay in the population dynamics. On the other hand, molecular dynamics simulations indicate that the quantum coherent effects in a single FMO were larger than expected because of an increase in the coupling strength attributable to the influence of the other monomers of the trimer[51]. Despite this, they[51] hypothesized that fast site-energy fluctuations (for example, due to thermal effects) are the main source of efficient transport, not the coherent quantum effects predicted by other studies.

Open problems. The observation at room temperature of quantum effects in a biological system[14–17] is itself remarkable. A great deal of evidence does suggest that in principle such coherence can enhance the efficiency of photosynthetic units, such as the FMO complex, even if just by a few per cent. Still, more work remains to be done to completely understand and validate this role. For example, no *in vivo* observations of coherence have yet been performed. In experiments, the excitations are created with laser pulses. *In vivo*, the excitations are generated by incoherent sunlight or through energy transfer from another antenna complex. Does quantum coherence still play a significant role in this situation? In addition, it is not yet clear whether the small enhancement in efficiency predicted by the quantum models provides a biological advantage[4,45]. Certain species, such as green sulphur bacteria or algae, live in very low-light conditions[15]. In such cases, any small enhancement in efficiency may be biologically important.

In higher plants the photosynthetic apparatus tends to be more complex and seems in some ways less ordered. This suggests that the energy landscape of these complexes is very rugged[15]. Thus, it may be that the quantum coherence seen in FMO plays an even more important role in maintaining high transport efficiency in such complex systems. Observation and validation of this hypothesis is one of the largest open problems in this field. For example, recent work[52] applied a renormalization analysis and found results that suggest the coherence in larger networks is limited by static disorder and not thermal effects. Similarly, an investigation[53] of the excitation transfer dynamics in the large chlorosome antenna of green sulphur bacteria found that the disordered energy landscape washed out all excitonic coherences. Inevitably, a broader understanding of the role of coherence in a larger range of photosynthetic complexes and organisms (for example, LH-1, LH-2 and LHCII) is needed. Typically, robustness[54,55] and photoprotection[56,57] are thought to be more of a natural necessity, rather than high efficiencies.

Avian magnetoreception

Magnetoreception is the ability of some migrating species to navigate using the Earth's magnetic field. The precise mechanism used, and its features, seem to vary greatly from animal to animal. A mechanism based on magnetite, deposits of magnetic iron minerals, has been used to describe this ability in some organisms[58] (although recent reports suggest that, at least in pigeons, these deposits are in fact macrophages and play no role in the magnetic sense[59]). However, behavioural experiments on other organisms seem to rule out the magnetite-based mechanism. For example, European robins have a magnetic sense that acts as an inclination compass insensitive to polarity[60], whereas most (although not all) magnetite-based compass models operate as a polarity-sensitive sense[58].

A series of behavioural experiments have revealed several more intriguing properties of this non-polar magnetic sense. Again, in European robins (and some other species) the navigation sense was shown to be photoreceptor based, that is, dependent on the presence of certain frequencies of ambient light[58,61]. It was also shown to be sensitive to changes in the intensity of the external magnetic field[58,62], but that it readjusted over time to these changes[62,63]. Finally, it has been shown that the navigation sense was disrupted by magnetic pulses[64], and very weak external oscillating magnetic fields[65].

In response to the early experiments showing the light-dependent properties of magnetoreception, Schulten *et al.*[66] proposed the radical-pair mechanism as a plausible biological chemical-compass. It was already well known that radical pairs can mediate magnetic-field-sensitive and light-activated chemical reactions, but up to that point only with external fields much stronger than the Earth's. The standard radical-pair model can be summarized as follows, although the exact details and steps involved can be quite complex: a radical pair is (typically) a pair of bound molecules that each has an unpaired electron. These pairs are created, by a photochemical process, in spin-correlated states; that is, singlets or triplets. The state of these spins then evolves under the combined effect of the Earth's weak magnetic field and internal nuclear hyperfine interactions with the host nuclei. Finally, the rate of charge recombination depends on the spin of the separated charges, directly influencing the reaction products of these radical pairs. These differing reaction products are in principle biologically detectable. Thus, if the relative weights of the singlet and triplet states are sensitive to the angle of the external (geo-magnetic) field, the reaction products will be also, leading to a magnetic compass.

The precise nature of the radical pair that might be involved in this mechanism is as yet unknown. The prime suspect is a series of radical-pair reactions that are known to occur within cryptochromes[67,68], which, because they are resident in the eye, could induce a visual signal by which the host species navigates. Simple models[69] of these kinds of radical pair, using highly anisotropic nuclear spin configurations, are sufficient to show that in principle the radical-pair reaction products are sensitive to the inclination of the external field, and can reproduce the disruptive effect of time-dependent external magnetic fields at radio frequencies.

Quantum properties. How then might this mechanism be described as an example of quantum biology? Although spin singlet (S_0) and triplet (T_0) states are certainly ubiquitous in atomic and molecular physics, they are also some of the most quantum of states. The T_0 and S_0 states are equivalent to Bell states, maximally entangled states that are highly desired in quantum information schemes. How much of a role does the quantum nature of these states play in this mechanism? A recent analysis of the lifetime and decoherence of these states in the radical-pair mechanism[70] suggests that the answer is quite complex. Essentially, some dephasing models leave the sensitivity of the radical-pair reactions to the external fields mostly intact. However, any kind of strong dephasing prevents the radical-pair model from being able to explain the disruptive effects of very weak oscillating fields. In addition, because these disrupting fields were so weak, of the order of 50–100 nT, they

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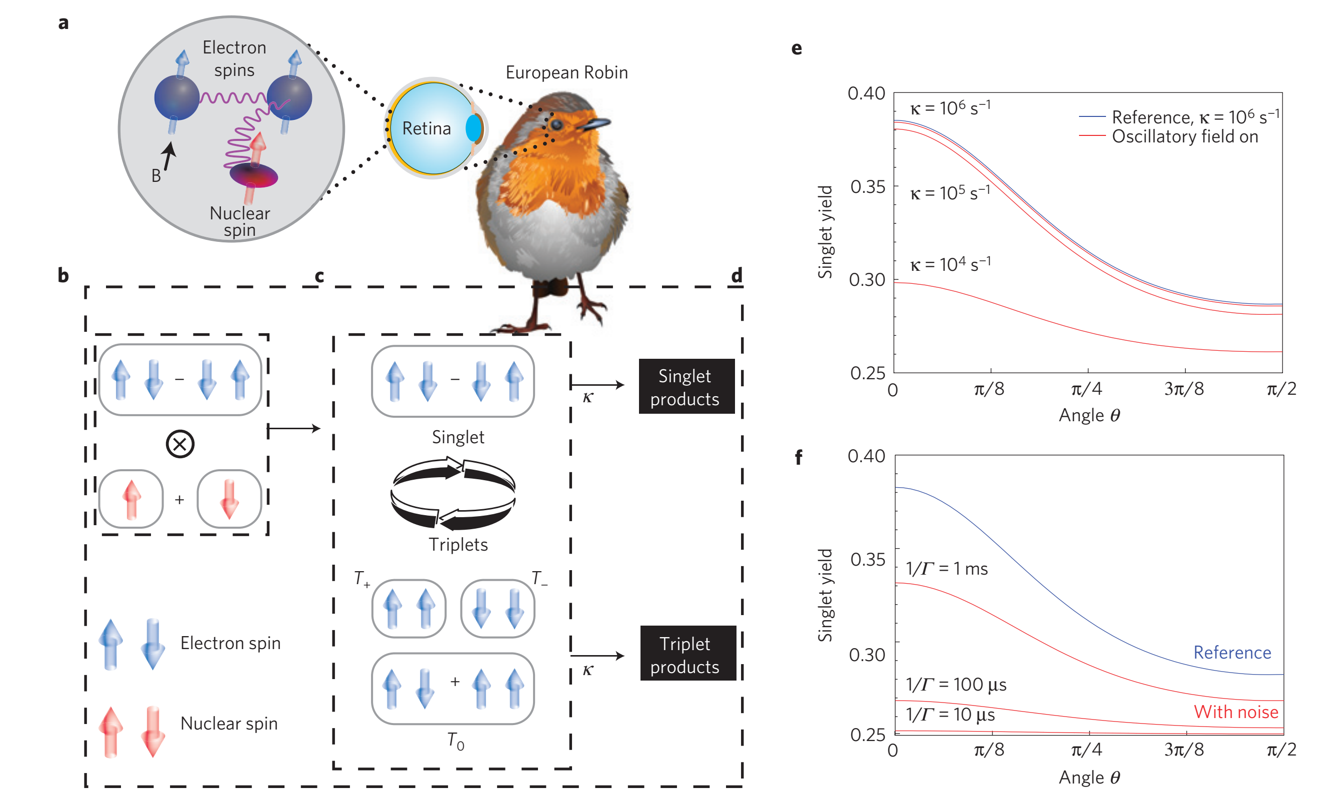


Figure 2 | The avian quantum compass. The radical-pair mechanism for avian magnetoreception explains many of the behavioural studies performed on some species of migrating birds. Key properties of the proposed radical-pair model for avian magnetoreception are dependent on quantum mechanics; therefore, this may represent a functional piece of biological quantum hardware. **a**, A schematic of the radical-pair mechanism for magnetoreception that could potentially be employed by European robins and other species. It is thought to occur within cryptochromes, proteins residing in the retina. There are three main steps in this mechanism. First, light-induced electron transfer from one radical-pair-forming molecule (for example, in a cryptochrome in the retina of a bird) to an acceptor molecule creates a radical pair. **b**,**c**, Second, the singlet (S) and triplet (T) electron-spin states inter-convert owing to the external (Zeeman) and internal (hyperfine) magnetic couplings. **d**, Third, singlet and triplet radical pairs recombine into singlet and triplet products, respectively, which are biologically detectable. **e**, Singlet yield (a measure of the probability of the radical pair to decay into a singlet state) as a function of the external-field angle θ in the presence of an oscillatory field (taken from Gauger *et al.*[70]). The blue top curve shows the yield for a static geomagnetic field ($B_0 = 47\,\mu$T), and the red curves show the singlet yield in the case where a 150 nT field oscillating at 1.316 MHz is superimposed perpendicular to the direction of the static field. The sensitivity of the compass can be understood as the difference in the yield between $\theta = 0$ and $\theta = \pi/2$. An appreciable effect on this sensitivity occurs once κ (the decay rate of the radical) is of order 10^4 s^{-1}. **f**, Singlet yield as a function of the magnetic field angle θ for differing noise magnitudes (from Gauger *et al.*[70]). The blue curve shows the optimal case with no noise (but with decay rate $\kappa = 10^4$ s^{-1}). The red curves indicate that a general noise rate of $\Gamma > 0.1\kappa$ has a detrimental effect on the sensitivity. Both of these results indicate that the electron spin state must have a remarkably long coherence time.

demand that the radical-pair model maintain quantum coherence of its spins for tens of microseconds (see Fig. 2). It seems then that this disruption due to external fields is a purely quantum effect, and that both the quantum coherence and entanglement properties must be sustained for timescales 'exceeding the best man-made molecular systems'[70]. Ironically, although these experiments with disruptive time-dependent fields are some of the best evidence so far for the radical-pair model, they also set challenging criteria for spin coherence and radical-pair lifetimes to match.

Recent progress. There is a long history of experimental studies of magnetic-field sensitivity on radical-pair reactions in solution[71]. However, in those early experiments sensitivity was observed only for field strengths between 10 mT and several tesla, much larger than Earth's (~50 μT). Within the past decade, the observed sensitivity of such reactions has gradually increased. Woodward *et al.*[72] studied the photoactivated reaction of pyrene and *N*,*N*-dimethylaniline in solution, and applied external oscillating fields of order ~500 μT. This resulted in a change of concentration of reaction products of 25%. Maeda *et al.*[73] reported the most sensitive radical-pair reaction so far: a triad composed of linked carotenoid (C), porphyrin (P) and fullerene (F). They found magnetic field sensitivities down to 50 μT, of the same order as the geomagnetic field. However, there was an angular dependence (between the molecule and the externally applied field) only for stronger field strengths, of the order of milli-tesla.

As mentioned earlier, cryptochrome, a ubiquitous photoactive protein that resides in the eye and is also present in plants and bacteria, is a prime candidate as the host of the radical-pair mechanism. Ritz *et al.*[67] originally proposed that it may play a role as the host of the magnetically sensitive radical-pair reaction. Very recent results[7] (again *in vitro*) have successfully shown magnetically sensitive radical-pair reactions in a cryptochrome extracted from the plant *Arabidopsis thaliana*. They saw a change in yields of order 25% at 30 mT and 1% at 1 mT. Although this is still much larger than the geomagnetic field, the authors speculate that the response *in vivo* may be much stronger.

The question of how the sensitivity might be maximized by different configurations and parameters within the radical-pair model has also been addressed in recent theoretical work. Cai *et al.*[74] argued that in fact a highly anisotropic but weak nuclear hyperfine interaction is preferable, and produces the overall maximum for

reasonable choice in radical-pair lifetimes. Most other studies have used a stronger choice of nuclear hyperfine coupling. In addition, recent works[70,74] discuss the effect of environmental noise on the sensitivity and, as mentioned earlier, illustrate that the behaviour can be counter-intuitive. One proposal[75] argued that the behavioural experiments strongly suggest that quantum coherence is present within the radical-pair compass, but to a degree that is not actually required for normal functioning of the compass. To explain why high levels of quantum coherence might be useful, they suggested a modified, and rather speculative, version of the radical-pair model. In their new scheme, a biologically detectable signal is not given by reaction products but by a long-lived dipole moment. In their proposal, the quantum coherence improves the sensitivity to external fields in a very direct way.

Recent results show that pigeons have an identifiable neural substrate for processing magnetic sense information[76]. This substrate was shown to respond to several different kinds of magnetic sense information: direction, intensity and polarity. In addition, previously it was thought[77] that the magnetic sense of pigeons was mediated by magnetite deposits in their beaks. However, further work[59] has recently shown that these deposits are in fact a kind of macrophage, and play no role in the magnetic sense. These results do not directly affect the implications of the radical-pair model, as it was already well known that pigeons have a polarity-based sense. However, it does indicate that similar experiments on the neural properties of organisms in which the radical-pair model is hoped to exist are vital, and may shed further light on whether radical pairs do or do not play a role in magnetoreception.

Open problems. The main obstacle to verification of the radical-pair model is to show that cryptochromes (a host for radical pairs in the eye[67,68]), or some other candidate radical pair, have the right properties to respond to the extremely weak geomagnetic field[7,63,68]. To do so they must have a sufficiently long lifetime ($\geq 1\,\mu$s), and a sufficiently anisotropic nuclear spin coupling (or some other anisotropic mechanism to couple the singlet and triplet states). An obvious next step is to show that a radical pair, such as cryptochrome, can exhibit sufficient sensitivity to external fields in conditions that mimic those that might occur *in vivo*[7].

Another demanding aspect is the even longer lifetime and low environmental noise, or spin dephasing, that seem to be needed to explain the disruptive effects due to weak radiofrequency fields observed in behavioural experiments (see Fig. 2). As mentioned, this disruptive effect has been seen in robins[65,78] for fields as weak as 50 nT. Typically, the effect of such a weak field can be observed only on a timescale of 100 μs, demanding that the radical pairs must have an equally long coherence time. A recent theoretical work[79] hypothesized that a lifetime of 5 μs is sufficient to explain these experiments. Their argument was based on the observation that, in a theoretical model, the weak oscillating field can cause a small change in the overall singlet yield. A similar change occurs when an additional static field is applied. By comparing this observation to some behavioural experiments that observed magnetic sense disruption when static fields[62,63] were applied, they argue that there is a small window of operation (in terms of magnitude of singlet yield) outside of which the sense becomes disrupted.

Apart from these microscopic studies, one may imagine several more complex behavioural experiments to bolster the evidence for the radical-pair model[63,68]. One intriguing possibility is that of applying quantum control to mimic the effect of the static field. An appropriate choice of time-dependent external fields should, in principle, have the same effect on the radical-pair model as the static fields[74,80]. If it could be shown that the birds are able to respond to the encoded directional information in these oscillating fields, this would strongly imply that the radical-pair model does play a role. Such effects would be almost impossible to describe using any other magnetic field transduction mechanism. Thus, an experimental example of quantum control of birds would represent strong evidence in favour of the radical-pair scheme.

Finally, almost nothing is known about the biological circuitry connecting the radical-pair yield to a neurological signal. Some proposals[67,69] argue for an optical/visual signal, particularly because of the role cryptochromes may play. However, a deeper understanding of the chain of events connecting the singlet/triplet yield to a neurological signal is vital to understand why the magnetic sense (if it is transduced by radical pairs) is so sensitive to small changes in this yield.

Other quantum biological systems

Apart from photosynthesis and magnetoreception there are already several other biological processes in which quantum effects are thought to play a vital but more indirect role. In this section, we examine briefly a few of these examples.

Tunnelling in biological systems. Tunnelling of light-mass particles is a quintessential quantum effect well studied even at the dawn of quantum physics. In biology, it is evident that long-range electron tunnelling[81–83] and hydrogen tunnelling[84,85] play important roles in biological redox reactions and enzyme catalysis, respectively. Experimental data[81,86] have clearly demonstrated that long-range electron transfer between redox centres in proteins separated by distances of the order of 15–30 Å plays important roles in respiration and photosynthesis. These processes could depend critically on the specific electron transfer pathways encoded in the protein structures and specific intermediate relays in the amino-acid sequences[81,86,87].

Observations of long-range electron transfer through proteins often show exponential distance dependence as well as weak temperature dependence[81,83], providing a strong indication that a single-step tunnelling mechanism is responsible for these biological processes. It is remarkable that such long-distance electron transfer in biology occurs through quantum mechanical tunnelling, because electron tunnelling over such long distances would be impossible in vacuum. Still, whether or not the electron-conducting proteins have evolved specifically for coherent electron tunnelling remains a major open question[81,86,87]. Quantum theory predicts that electron transfer pathways could interfere with one another, and there is evidence that electron transfer through the azurin protein depends critically on quantum interferences between multiple distinct pathways[88,89]. Several recent works[90,91] proposed a molecular which-way interferometer experiment in which localized normal modes coupled to bridge atoms can be vibrationally excited to control interferences between transfer pathways. Such experimental probes of pathway coherence in electron-transfer proteins in a single-protein level would provide decisive proof for the quantumness of the electron tunnelling process. In addition, another biological function that might depend on electron tunnelling concerns our sense of smell. Recent experimental data suggest that the traditional models of a docking-type mechanism, based solely on the size and shape of odorant molecules, is inadequate to explain our sensitivity of olfaction. Turin[92] proposed a mechanism in which phonon-assisted inelastic tunnelling of an electron from a donor to an acceptor mediated by the odorant molecule gives a further level of selectivity to the process. A recent model proposed by Brookes[93] expanded on this idea, and presented evidence that such a mechanism fits the observed features of smell. However, it should be noted that their model is semi-classical, and does not depend directly on quantum coherence or superposition. Thus, so far it sits on the border of what might be classified as quantum biology.

Hydrogen tunnelling also plays an important role in a wide range of biological enzymatic catalytic reactions[84,85]. Observations

of strong intrinsic kinetic isotope effects in enzymatic reactions have clearly demonstrated nuclear quantum effects in enzymes[84,85]. However, in enzyme catalysis, a large portion of the quantum improvement over the classical catalytic rates could be attributed to the zero-point energy that gives a quantum correction to the barrier height and the hydrogen tunnelling rates[85]. Such nuclear quantum effects actually represent a class of quantum phenomena in biological systems that depends only on trivial quantization and discrete energy levels, not quantum coherence.

Photoreceptors. For the survival of many organisms, the ability to sense and respond to various light conditions through light-sensing proteins plays a crucial role. Such biological photoreceptors contain chromophores that absorb photons and then undergo rapid chemical transformation on their excited states, eventually leading to light-induced signal transduction[94,95]. Owing to the quantum nature of electronically excited states and nuclear quantum coherences that often accompany excited-state molecular dynamics, quantum mechanics is required to describe these photoactivated dynamics in biological photoreceptors[96].

The prototypical example here is the trans-membrane protein called rhodopsin that is responsible for the primary event in vision. Rhodopsin contains a retinal molecule that undergoes photoisomerization following light absorption. This photoisomerization reaction[97] proceeds with remarkable rate (<200 fs, one of the fastest chemical reactions known) and high specificity (quantum yield of ~ 0.65). It then triggers a protein conformational change that is subsequently amplified by signal-transduction proteins, leading to the visual signal. The remarkably rapid and efficient photoactivated one-way reaction dynamics in rhodopsin is a result of the ultrafast coherent wave-packet dynamics that depends critically on the quantum mechanical positioning of the excited-state potential energy surfaces and the symmetries of the electronic states[94,95,98–100]. In these systems, nature most likely uses trivial quantum effects to shape the ground-state and excited-state potentials of the photoreceptors to achieve high specificity and yield.

Evidence of quantum-coherent effects (for example, the interference between wave packets) in photoisomerization of natural photoreceptors is still lacking. Intriguingly, coherent optical control of retinal isomerization in bacteriorhodopsin, a protein related to vertebrate rhodopsins, has been demonstrated experimentally[101,102]. Although this is directly relevant only to experiments with lasers, it is interesting to determine whether coherent light can be used to take advantage of the quantum nature of the photoreceptors to direct chemical dynamics through coherent interferences of nuclear wave packets to achieve even higher reaction yields.

Conclusions

Here, we return to the question we posed in the introduction to this short review, has nature already beaten us in leveraging quantum effects to achieve something an equivalent classical system cannot? Certainly nature can harvest energy extremely efficiently, sense weak magnetic fields and create human minds complex enough to even be asking these questions. Now preliminary evidence suggests that nature may also leverage quantum effects to enhance the efficiency, or functionality, of some of these amazing feats. There is some evidence of room-temperature quantum effects (superposition and coherence) on physically important timescales in the electronic excitation transfer process in photosynthesis. Theoretical models suggest that this may enhance the overall efficiency of this transport, although larger or more complex systems need to be studied in more detail to ascertain both how vital and universal this enhancement is.

In the case of the avian magnetoreception, if the interpretation of behavioural experiments on certain avian species is correct, then it could be that the ability of these species to navigate by the Earth's magnetic field is transduced by a magnetically sensitive chemical reaction that relies on certain subtle quantum effects. Strong evidence in favour of this model could come from further *in vitro* experiments on candidate radical pairs that show anisotropic sensitivity to very weak magnetic fields, or more sophisticated behavioural experiments. Finally, there are already a range of other functional biological systems that may rely on processes that can be thought of as fundamentally quantum (although as yet in a less direct way than magnetoreception and photosynthesis).

The fact that there is even the possibility of a functional role for quantum mechanics in all of these systems suggests that the field of quantum biology is entering a new stage. There may be many more examples of functional quantum behaviour waiting to be discovered. In addition, there are several obvious broader questions that arise: can we learn from nature's example and develop bio-mimetic quantum technologies for efficient energy harvesting, long-coherence-time chemical reactions and so on? Alternatively, if it turns out that non-trivial quantum coherent effects do not play a strong functional role in biology, then this begs the question 'why not?' Are all quantum effects destroyed or limited by the hot and wet biological environment, or do these quantum effects simply not provide a biologically significant advantage over classical equivalents?

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Competing financial interests

The authors declare no competing financial interests.